

REPORT DOCUMENTATION PAGE

Public reporting burden for this collection of information is estimated to average 1 hour per response, including gathering and maintaining the data needed, and completing and reviewing the collection of information. Send collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork

G559

yes,
this
son

1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE		3. REPORT TYPE AND DATES COVERED FINAL 15 Apr 93 To 14 Sep 96	
4. TITLE AND SUBTITLE THEORETICAL MODELING OF OCULAR TISSUE DAMAGE BY SHORT PULSE LASERS				5. FUNDING NUMBERS F49620-93-1-0298 2312/AS 61102F	
6. AUTHOR(S) DR STEVEN L. JACQUES					
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) MD Adderson Cancer Center University of Texas 1515 Holcombe Boulevard Houston TX 77030				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) AFOSR/NL 110 Duncan Ave Room B115 Bolling AFB DC 20332-8050 Dr Walter Kozumbo				10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES					
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for public release; distribution unlimited.				12b. DISTRIBUTION CODE	
13. ABSTRACT (Maximum 200 words) This work has developed computer simulations of how ultra-short pulsed lasers will interact with the retina. Consideration was given to how optical energy couples into the melanosomes of the retinal pigmented epithelium (RPE), how thermal energy is confined within the melanosomes, how stress is generated in the melanosomes, and the pulse-duration dependence of thermal and stress induced injury to the melanosome.					
14. SUBJECT TERMS				15. NUMBER OF PAGES	
				16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT (U)		18. SECURITY CLASSIFICATION OF THIS PAGE (U)		19. SECURITY CLASSIFICATION OF ABSTRACT (U)	
				20. LIMITATION OF ABSTRACT (UL)	

19971103 081

Report type Final Technical Report
Number F49620-93-1-0298 (or FA9620-93-1-0298)
PI Steven Jacques
PM NL/Berry
Due Date Nov 14, 1996
DODAAD CODE OKD38
Institution University of Texas M.D. Anderson Cancer Center

(AFOSR) Air Force Office of Scientific Research (FA9620-93-1-0298)
PI: Steven L. Jacques
Laser Biology Research Laboratory
University of Texas M.D. Anderson Cancer Center
4/15/93 - 4/14/96
Annual Direct Costs: \$33,783 (TOTAL AWARD: \$150,000)
THEORETICAL MODELING OF OCULAR TISSUE DAMAGE BY SHORT
PULSE LASERS

Current address:

Steven L. Jacques, Ph.D.
Oregon Medical Laser Center
Providence St. Vincent Medical Center
9205 SW Barnes Rd
Portland, OR 97225
503-216-4092
503-216-2422 fax
sjacques@ee.ogi.edu
<http://ee.ogi.edu/omlc>

Copy available at <http://ee.ogi.edu/~sjacques/reports/afosr96.html>

FINAL TECHNICAL REPORT

This work has developed computer simulations of how ultra-short pulsed lasers will interact with the retina. Consideration was given to how optical energy couples into the melanosomes of the retinal pigmented epithelium (RPE), how thermal energy is confined within the melanosomes, how stress is generated in the melanosomes, and the pulse-duration dependence of thermal and stress induced injury to the melanosome.

We studied the hypothesis that ultra-short laser pulses (< 100 ps) will disrupt melanosomes by the mechanism of tensile stresses. Dense 10-nm granules stud the membrane walls within the melanosome. Ultra-short pulse lasers deposit energy in the granules faster than stress can escape each granule at the speed of sound. The stress is generated in each granule by thermoelastic expansion. Without release, the stress will build up to high pressures then radiate as high pressure stress waves. When such stress waves cross granule/water interfaces, or on the larger scale of 1-2 μ m melanosomes when stress waves cross

melanosome/cytosol interfaces, the mismatch in mechanical impedance generates tensile stresses (negative value) which exceed the cavitation threshold for soft tissue, about -10 to -30 bars. The cavitation causes disruption of melanosomes. The Minimal Visible Lesion (MVL) threshold for retinal injury for laser pulses below 100 ps begins to drop below the threshold based on simple explosive vaporization of melanosomes due to generation of water vapor. This drop in MVL begins at 100 ps and drops roughly 10-fold at increasingly shorter pulses extending into the 100 fs regime. This 10-fold magnitude is consistent with the predictions of the hypothesis of a tensile stress mechanism of melanosome disruption secondary to stress confinement in melanosomal granules.

We began to coordinate our work with the AFOSR-sponsored research of Randy Glickman, Ph.D., and the Univ. of Texas Health Science Center at San Antonio, Dept. of Ophthalmology. His work has studied oxidative damage to the RPE caused by melanosomes when exposed to blue light. We jointly explored the hypothesis that laser-disrupted melanosomes would expose the melanin of the melanosomal interior to the cytosol of the cell, then subsequent blue light exposure would activate the melanin to cause oxidative injury to the cell which in turn would lead to cell death and an observable MVL.

We disrupted melanosomes isolated from the bovine RPE using a Q-switched doubled-Nd:YAG pulses (10 ns, 532 nm). The disrupted melanosomes were then irradiated by blue light (argon laser, 480 nm) to activate the melanin photochemically so that it oxidized a test substrate (NADPH). We demonstrated that laser disruption of melanosomes enhances melanosome-mediated oxidation of NADPH, assayed spectrophotometrically. NADPH oxidation is a model system for oxidative injury to the components of the cell cytosol. Our finding supported the hypothesis that laser-disrupted melanosomes increase the susceptibility to retinal injury by blue light exposure.

The practical conclusions of our studies are:

(1) After acute pulsed laser injury, there may be a risk factor associated with ocular exposure to blue light, for example the blue light in sunlight or artificial lighting. Such blue light exposure may exacerbate the initial laser injury.

(2) Ultra-short laser pulses (< 100 ps) may cause melanosome disruption via tensile stresses that elicit cavitation. Such disruption would then enable the above susceptibility to blue light oxidative injury. This hypothesis is consistent with the reported 10-fold drop in MVL for laser pulses below 100 ps.

PUBLICATIONS:

We have reported our work in the following conference and journal papers and are submitting our conference papers to peer-reviewed journals for publication.

S.L. Jacques, A. Oraevsky, R. Thompson, B. Gerstman: Working theory and experiments on photoacoustic disruption of melanosomes to explain the threshold

for minimal visible retinal lesions for sub-ns laser pulses. *SPIE Proceedings* 2134:54-65, 1994.

C.R. Thompson, B.S. Gerstman, S.L. Jacques, M.E. Rogers: Melanin granule model for laser-induced thermal damage in the retina, *Bull. Math. Biol.* 58:513-553, 1996. [published erratum appears in *Bull. Math. Biol.* 58:809-10, 1996.]

B.S. Gerstman, S.R. THompson, S.L. Jacques, M.E. Rogers: Laser induced bubble formation in the retina, *SPIE Proceedings* 2391:60-71, 1995.

B.S. Gerstman, S.R. THompson, S.L. Jacques, M.E. Rogers: Laser induced bubble formation in the retina. *Lasers Surg. Med.* 18:10-21, 1996.

S.L. Jacques, R.D. Glickman, J.A. Schwartz: Internal absorption coefficient and threshold for pulsed laser disruption of melanosomse isolated from retinal pigment epithelium. *SPIE Proceedings* 2681:468-477, 1996.

R.D. Glickman, S.L. Jacques, J.A. Schwartz, T. Rodriguez, K. Lam, G. Buhr: Photodisruption increases the free radical reactivity of melanosomes isolated from retinal pigment epithelium. *SPIE Proceedings* 2681:460-467, 1996.

R.D. Glickman, B.A. Rockwell, S.L. Jacques: Action spectrum of oxidative reactions mediated by light-activated melanin. *SPIE Proceedings* 2975:138-145, 1997.